

Oral Testimony Before the CASAC Ozone Review Panel on the Third Draft Ozone ISA

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Thank you for the opportunity to speak on behalf of the American Forest and Paper Association. I will be focusing on two issues in the third draft ozone ISA (US EPA, 2012): EPA's weight-of-evidence approach and its evaluation of controlled exposure studies.

The National Research Council Formaldehyde Review Panel called on EPA to undertake a program to develop a transparent and defensible methodology for weight-of-evidence assessments (NRC, 2011). The Panel's report contains a "roadmap" for reform and improvement of the risk assessment process. While the Panel did not specify methods to be adopted, it used the PM ISA approach (which is the same as the ozone approach) as an example of a useful model for providing insights that EPA could use to formulate a more rigorous approach. There are some factors specified in this framework, such as the consideration of Bradford Hill's "aspects" and weighing of alternative views on controversial issues, that are crucial for any weight-of-evidence analysis. There are other features, however, that are lacking. In addition, although EPA claims to use this framework in the ozone ISA, certain parts of the framework are not applied.

Regarding the issues with the framework itself, there are no clear statements in the ISA indicating how EPA applies the Bradford Hill aspects or how its causality judgments consider all aspects jointly. For example, the ISA says the strength of an association should be considered, but provides no indication of what constitutes a strong association. Most associations in the ozone epidemiology studies are weak (*i.e.*, most risk estimates are well below 2), and could be chance findings resulting from methodological limitations inherent in epidemiological studies. Therefore, a definition of "strong" is needed for the criterion for evaluating the methodological rigor of a study. EPA should also be more explicit in how it evaluates alternative hypotheses and the criteria it uses to determine which hypothesis is most supported by the data. It is not evident that EPA considers any hypothesis beyond ozone as a causal factor for specific health effects.

Regarding the application of the framework, perhaps the most serious issue is that studies are not always evaluated in a consistent manner; this is particularly the case for epidemiology studies. Sometimes a particular feature that is considered a limitation in one study is not mentioned in the discussion of another. For example, EPA states that a Girardot *et al.* (2006) study limitation is the outcome measurement, in that lung function measurements were taken by "less well-trained technicians," but EPA does not have a qualification for studies that rely on self-administered PEF, which has been demonstrated to be a highly unreliable outcome measurement. Studies with the most rigorous methods should be given the greatest weight in an analysis, but it is not clear whether or how individual studies are weighted in the ISA, based on these criteria. In general, rather than explicitly stating all results, the ISA highlights positive associations and often omits discussions of negative associations, making results seem more consistent than they actually are.

These issues are also apparent in Chapter 8 of the third draft ISA, where EPA introduces a new classification framework that it claims is a weight-of-evidence approach to identify and understand "at-risk" factors that cause an increased probability of ozone-related health effects. EPA says it uses this framework to assess the coherence of effects across disciplines and to determine the biological plausibility of these factors. There is no discussion, however, of a review protocol or literature search strategy, and no clear criteria for evaluating individual studies, including how methodological limitations and uncertainties are evaluated, or how results from different lines of evidence should inform the interpretation of each other. It is also not clear that all relevant data are discussed, as it appears that positive results are given more weight in the discussion. A true weight-of-evidence evaluation should only emphasize results based on the rigor of the methods used to obtain them, and not based on the results themselves.

Finally, I would like to briefly discuss the analysis of controlled exposure studies in the ISA. It does not appear that EPA has made any significant changes, despite the many scientific arguments put forth in response to the first two drafts. Most importantly, biological evidence supports a threshold mode of action by which ozone exposure over a sufficient duration and concentration overwhelms respiratory system antioxidants, resulting in oxidative damage. This is also supported by the most recent analysis of controlled exposure data by McDonnell *et al.* (2012), which found that threshold models best describe the data, particularly at the lower end of the exposure-response curve, which is most relevant to the NAAQS. EPA needs to acknowledge that the biology and controlled exposure studies clearly indicate a threshold.

In conclusion, the third draft ISA does not use an objective and rigorous weight-of evidence approach to evaluate ozone exposure and health effects data or evaluate the controlled exposure studies in a scientifically rigorous manner. EPA should follow the NRC Panel's recommendations for best practices in risk assessment to ensure EPA's goal of providing credible causal conclusions about ozone-related health effects in the final ISA. On behalf of American Forest and Paper Association, thank you for your consideration of these comments.

References

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